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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/770,467	02/04/2004	Bodo Plachter	966927-20002D	1358

7590 09/08/2006

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/770,467	PLACHTER, BODO	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29 and 31-33* is/are rejected.

7)☒ Claim(s) *26 and 30-32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is in response to the After-Non-Final amendment filed on 20 June 2006. Claims 1-25 have been cancelled. Claims 26-33 are newly added and pending.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 31 and 32 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,713,070. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims in the parent case anticipate the instant claims.

Both sets of claims are drawn to the same active ingredients, which are HCMV sub-viral particles.

Response to Arguments

Objections

The objection to the specification **is withdrawn** in view of the Applicant's amendment.

The objection to claims 15 and 19 **is withdrawn** in view of the Applicant's cancellation.

Claim Rejections - 35 USC § 112

The rejection of claims 15, 18 and 20 under 35 U.S.C. §112, second paragraph, as being indefinite **is withdrawn** in view of Applicant's cancellation of the claims.

Claim Rejections - 35 USC § 102

The rejection of claims 21, 23 and 25 under 35 U.S.C. §102(b) as being anticipated by Gibson *et al.* (1984) **is withdrawn** in view of Applicant's cancellation of the claims.

Claim Rejections - 35 USC § 103

The rejection of claims 15 and 16 under 35 U.S.C. §103 (a) as being obvious over Michel *et al.* (1996) in view of Wang *et al.* (US 5,830,727) **is withdrawn** in view of the Applicant's cancellation of the claims.

The rejection of claims 15, 17 and 18 under 35 U.S.C. §103 (a) as being obvious over Michel *et al.* (1996) in view of Wang *et al.* (US 5,830,727) and further in view of

Uyttersprot *et al.* (1998) **is withdrawn** in view of the Applicant's cancellation of the claims.

The rejection of claim 20 under 35 U.S.C. §103 (a) as being obvious over Michel *et al.* (1996) in view of Wang *et al.* (US 5,830,727) and further in view of Irmiere *et al.* (1983) **is withdrawn** in view of the Applicant's cancellation of the claims.

The rejection of claims 21 and 22 under 35 U.S.C. §103 (a) as being obvious over Gibson *et al.* (1984) in view of Wills *et al.* (1996) **is withdrawn** in view of the Applicant's cancellation of the claims.

New Claim Objections

Claim 26 is objected to because 26 part d) is missing the word "a" between "with" and "virus" and a comma at the end of the sentence.

Claim 30 is objected to for depending from a rejected claim.

Claim 31 is objected to for a grammatical error in part c), wherein the "sub-viral particle" should be in singular form to agree with the "a fusion protein" of the sentence.

Claim 32 is objected to for reciting acronyms "gB" and "gH" without first identifying the full names.

New Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 26, 27, and 33 are rejected under 35 U.S.C. §103(a) as being unpatentable over Michel *et al.* (1996) in view of Gibson *et al.* (1984).

The instant claims are drawn to a method for producing viral particles comprising the following steps: a) provision of a human cytomegalovirus (HCMV) in whose genome an essential gene has been deleted, b) transfection of a stably transfected mammalian cell line which expresses the HCMV gene deleted in a), c) replication of the gene-deleted virus from a) in cells from b), d) infection of mammalian cells with virus which has been replicated as in steps a) - c), e) isolation of viral particles from cells which have been infected as in step d), wherein f) the particles are surrounded by a lipid membrane in which viral glycoproteins are embedded, and g) the particles contain neither viral DNA nor capsids.

Michel *et al.* disclose an HCMV gene with the N-terminal region of UL97 deleted. The deleted HCMV is replicated in human foreskin fibroblasts. See page 6340, Materials and Methods. Michel *et al.* describe that the UL97-deficient recombinant viruses are growth defective, and therefore this gene may be essential for the HCMV life cycle. See page 6344, left column, the sentence above Discussion. Importantly, Michel *et al.* disclose that a cell line stably expressing the UL97 protein can act as a rescue system for UL97-deficient HCMV. See last sentence.

Michel *et al.* do not disclose isolation of viral particles.

Gibson *et al.* describe the isolation of noninfectious HCMV particles including dense bodies, which are devoid of capsids and contain less than trace amounts of viral DNA but contain all of the glycoprotein species present in virions. See page 321, last

paragraph. Gibson *et al.* specifically describe the use of the noninfectious viral particles as subunit vaccines, which encompass the claimed immunization composition with a pharmaceutical carrier.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the cell-rescue viral replication method of Michel *el al.* with the method of isolation of noninfectious viral particles, as taught by Gibson *et al.* to ensure the non-infectivity of HCMV viral particles. One having ordinary skill in the art would have been motivated to do this to develop additional diagnostic and therapeutic approaches to CMV-related diseases, as per the suggestion in Gibson *et al.* Thus, claims 26, 27 and 33 are *prima facie* obvious over Michel *et al.* in view of Gibson *et al.*

Claims 28 and 29 are rejected under 35 U.S.C. §103(a) as being unpatentable over Michel *et al.* (1996) in view of Gibson *et al.* (1984) and further in view of Uyttersprot *el al.* (1998).

The instant invention is further limited to a lipid-containing transfection agent.

The relevance of Michel *et al.* and Gibson *et al.* are set forth above. Michel *et al.* and Gibson *et al.* do not disclose the method step of cell transfection with a lipid-containing reagent. Uyttersprot *el al.* disclose the lipid formulation, FUGENE 6 transfection reagent. See entire document.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to add the FUGENE transfection reagent of Uyttersprot *et al.* to the combined methods of Michel *et al.* and Gibson *el al.* to improve the

efficiency of HCMV replication. One having ordinary skill in the art would have been motivated to do this so that mammalian cell transfection has increased uptake, as per the suggestion in Uyttersprot *et al.*, which will increase the yield of viruses with a reasonable expectation of success because Uyttersprot *et al.* specifically disclose successful transfection of human foreskin keratinocytes using the FUGENE 6 transfection reagent. Thus, claims 28 and 29 are obvious over Michel *et al.* in view of Gibson *et al.*, and further in view of Uyttersprot *el al.*

Claims 31 and 32 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gibson *et al.* (1984) in view of Plachter *et al.* (1990) and Wills *et al.* (1996).

The instant claim is drawn to a composition for immunization against HCMV diseases and infections comprising sub-viral particles and pharmaceutically acceptable carrier, wherein the sub-viral particles additionally contain a fusion protein comprising one or more parts of the T-cell antigen pp65 (UL83) and one ore more parts of one ore more proteins which are not pp65.

The relevance of Gibson et al. is set forth above. Gibson *et al.* do not describe a sub-viral particle containing a pp65 fusion protein.

Plachter *et al.* describe fusion protein resulting from fusing different fragments of the open reading frame coding for pp65 with fragments from purified lambda clones. See Abstract and Figure 2. Plachter *et al.* disclose propagation of the virus and purification of HCMV virions or dense bodies from infected primary human foreskin fibroblast cells. See p.1229, Materials and Methods. Plachter *et al.* specifically disclose

that pp65 has the potential to elicit an antibody response during natural infection. This protein is a major constituent of the virus particle and represents over 90% of the protein mass of dense bodies. See p.1229, left column, 2nd ¶. The tegument protein pp65 might be one major target of the cell-mediated immune response during natural infection with HCMV. It also causes a humoral immune response in animals as well as in humans. Most importantly, pp65 alone is not a reliable antigen to generate antibody reactivity but might be very helpful in combination with other antigens for the detection of acute stages of HCMV infections. See p.1234, last ¶. Therefore, Plachter et al. explicitly suggest fusing pp65 with another immunogen or epitope.

Reschke *et al.* describe humoral immune response to gpUL75 (gH) (Abstract) and constitutive expression of HCMV gH protein in astrocytoma cells (p.252, RESULTS).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the dense bodies of Gibson *et al.* by adding pp65 fused to the gH protein. One having ordinary skill in the art would have been motivated to do this so that the viral particles have increased immunogenicity by eliciting both humoral and CTL immune response. There would be a reasonable expectation of success, given that pp65 and gH proteins can be stably expressed in mammalian cell line, as taught by Plachter *et al.* and Reschke *et al.* Thus, claims 31 and 32 are obvious over Gibson *et al.* in view of Plachter *et al.* and Reschke *et al.*

Remarks

Claim 30 is apparently free of prior art of record. The close prior art, Michel *et al.* does not teach or fairly suggest deletion of the major capsids protein gene (UL86) from the HCMV genome.

Contact Information

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
30 Aug 2006

8/30/2006